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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
VOGEL, NANCY S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/655,914	BLATTNER ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-10 is/are pending in the application.

4a) Of the above claim(s) 1-4 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 5-10 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10 are pending in the application.

Election/Restrictions

Claims 1-4 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/11/05.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 5-10 of this application. There is no disclosure in the provisional application 60/409,089, of a method of preparing a culture of bacteria for transformation comprising culturing the bacteria to an optical density in excess of 1.0 in a medium using glycerol as a carbon source, and transforming the bacteria with a foreign DNA molecule. There is no disclosure of said method wherein the medium is Terrific Broth.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 10 is drawn to a method of preparing a bacterial culture for transformation comprising culturing the bacteria to an optical density in excess of 1.0 in a medium using glycerol as a carbon source, and transforming the bacteria with a foreign DNA molecule wherein transformants are recovered in excess of 10^{10} per microgram. Claim 10 is a genus claims in terms of a method of preparing any bacterial culture for transformation, such that the number of transformants recovered is greater than 10^{10} per microgram of DNA. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the methods of preparing bacterial cultures for transformation such that the recited transformation frequency is obtained. While the specification provides general information on the E. coli strain MDS41-R13, which has the property when subjected to the method of preparation recited in the claim, of yielding the recited result, there is no structure-function analysis of the strain useful for identifying other bacterial types which, when subjected to the recited method, would give the recited result.

Therefore, the specification does not describe the claimed method of preparing bacterial cultures in such full, clear, concise and exact terms so as to indicate that Applicant has possession of the method at the time of filing the present application. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of discovering it. The method itself is required. Thus, the written description requirement has not been satisfied.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preparing a bacterial culture of MDS41-R13 resulting in the recovery of transformants in excess of 10^{10} per microgram, does not reasonably provide enablement for methods of preparing a bacterial culture of other bacterial strains for transformation wherein the transformants are recovered in excess of 10^{10} transformants per microgram. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention: The nature of the invention is a method of preparing a bacterial culture, by growing the culture to a particular optical density (in excess of 1.0), in a medium using glycerol as a carbon source, such that a particular number of transformants, 10^{10} transformants per microgram of introduced DNA, results. Therefore, the invention is drawn to a method of high efficiency transformation of bacteria,

State of the prior art: The prior art taught that known methods of preparing a bacterial culture of E. coli for transformation, which is the most well studied bacterial transformation system, has been able to achieve at most $10^7 - 10^9$ colonies per microgram using the standard CaCl2 transformation method, and $10^9 - 10^{10}$ colonies per microgram using electroporation transformation methods. (see Pope et al., Nucleic Acids Research, 1996, Vol. 24 (3), 536-537, first paragraph, page 536). However, these high levels of transformation frequencies have not been reported for other bacteria. For example, using the claimed method of preparing a bacterial strain using the step recited in claim 5, i.e. culturing the bacteria to an optical density in excess of 1.0 in a medium using glycerol as a carbon source, the bacteria Agrobacterium tumefaciens was reported to yield 1-3 x 10^8 transformants per microgram (Mersereau et al, Gene 90 (1) 149-151 (1990)) (see abstract, see page 150, columns 1-2). Rates of transformation disclosed by Wirth et al. (Mol. Gen. Genet. 216:175-177, 1989) were much lower for a number of gram negative bacteria (see Table 1). Therefore, the prior art does not disclose that levels of transformation such as 10^{10} per microgram were routinely possible for bacteria.

Level of predictability in the art: The art teaches that even in the most well studied microorganism, ie E. coli, there is unpredictability in transformation efficiencies and reproducible results are difficult to achieve (Hengen, Trends in Biochem. Sci., 19:426-427 (1994) and Trends in Biochem. Sci. 21:75-76, 1996). Transformation competence is variable from strain to strain of E. coli hosts (Hanahan, US 4,851,348).

Existence of working examples: The specification discloses a single example of the method of preparing a single bacterial culture (E. coli strain MDS41-R13) for transformation, comprising culturing the bacteria to an optical density in excess of 1.0 in a medium using glycerol as a carbon source, in which transformants are recovered in excess of 10^{10} transformants per microgram (page 28 of the specification). Results for a comparison strain E. coli MG1655 did not yield the recited number of transformants (page 28). Therefore, a method of preparing a single type of E. coli bacteria for transformation wherein the frequency of transformation was in excess of 10^{10} transformants/ microgram was disclosed.

Breadth of claims: The claim is very broad, since it drawn to a method of preparing a culture of any bacteria for transformation, wherein transformants are recovered in excess of 10^{10} transformants per microgram of input DNA.

Amount of guidance provided by applicants: The amount of guidance for the method of preparing bacterial cultures for improved levels of transformation is small, since there is no guidance provided for obtaining the recited level transformation efficiency for any bacteria other than the E. coli strain MDS41-R13.

Amount of experimentation necessary to make and/or use the invention: It would require a large amount of unspecified experimentation to practice the invention as claimed since as described above, the levels of transformation recited in the claim is very high, and one of ordinary skill in the art could not predict what conditions would have to be used in order to obtain such high levels of transformation using any particular bacteria.

For these reasons, it is considered that it would require undue experimentation to practice the invention as claimed throughout its scope.

Claims 5-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 and by dependence, claims 6-10, are vague and indefinite in the recitation of "an optical density in excess of 1.0", since a wavelength is not specified at which the optical density is to be measured. Therefore, one cannot determine the intended metes and bounds of the claimed subject matter. Furthermore, the claim is vague and indefinite in the recitation of "a method of preparing a bacterial culture for transformation at increased efficiency", since it is not known to what the recited efficiency is being compared.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Mersereau et al (Gene, 90 (1990) 149-151).

Mersereau et al. disclose a method of preparing a bacterial culture for transformation comprising culturing the bacteria to an optical density of in excess of A600= 1 using TB medium, which contains glycerol as a carbon source, and transforming the bacteria with a foreign DNA molecule. The culturing is done at 30 C. See page 150, first column, first complete paragraph – second column, first complete paragraph.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NANCY VOGEL, PH.D.
PATENT EXAMINER